

REMARKS

The above amendments to the claims are being made in order to eliminate multiple dependency and for the purpose of reducing the filing fee. Please enter this amendment prior to calculation of the filing fee in this case.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with Markings to Show Changes Made."

Favorable consideration and allowance are earnestly solicited.

Respectfully submitted,
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claims 5-10, 17-19, 42, 53, 59, and 65-67 have been amended as follows:

5. (Amended) A polynucleotide according to claim 1, wherein the complementary strand of said polynucleotide hybridizes, under stringent conditions, with a polynucleotide-
~~according to any of claims 2 to 4~~ comprising the coding sequence as shown in SEQ ID NO:1.

6. (Amended) A polynucleotide according to claim 1 and comprising a nucleotide sequence which is ~~degenerate to the nucleotide sequence of a polynucleotide according to any of claims 3 and 4~~ encoding a polypeptide comprising the amino acid sequence as shown in SEQ ID NO:2.

7. (Amended) A polynucleotide according to claim 1, said polynucleotide comprising the complementary strand of a polynucleotide ~~according to any of claims 2 to 6~~ for which the coding sequence is as shown in SEQ ID NO:1.

8. (Amended) A polynucleotide according to ~~any of the preceding claims~~ claim 1 operably linked to a further polynucleotide comprising nucleic acid residues 5377 to 8527 of SEQ ID NO:1, corresponding to a 3' untranslated region, or a fragment thereof, or SEQ ID NO:1.

9. (Amended) A recombinant DNA molecule in the form of an expression vector comprising an expression signal operably linked to a polynucleotide ~~according to any of claims 1 to 7~~ claim 1.

10. (Amended) A host organism transfected or transformed with the ~~polynucleotide according to any of claims 1 to 8,~~ or the vector according to claim 9.

17. (Amended) Polypeptide according to ~~any of claims 14 to 16~~ claim 14 operably linked to the mature part of PAPP-A2 corresponding to amino acid residues 234 to 1791 of SEQ ID NO:2.

18. (Amended) Polypeptide according to ~~any of claims 12 to 17~~ claim 12, wherein said polypeptide is a recombinant polypeptide.

19. (Amended) Polypeptide according to ~~any of claims 12 to 18~~ claim 12, wherein the polypeptide is free of human proteins, or other proteins natively associated with said polypeptide.

Claims 20 and 21 have been cancelled.

22. (Amended) A method for producing an antibody with specificity for the polypeptide according to claim 12, said method comprising the steps of

- i) providing a host organism,
- ii) immunizing the host organism with the polypeptide according to ~~claim 10~~ claim 12, and
- iii) obtaining said antibody.

26. (Amended) A method for producing the polypeptide according to claim 18, said method comprising the steps of

- i) providing a suitable host organism,
- ii) ~~transfecting or transforming the host organism provided in step i) with the polynucleotide according to any of claims 1 to 8, or the vector according to claim 9~~transfecting or transforming the host organism with an expression vector, said vector comprising an expression signal operably linked to a polynucleotide encoding said polypeptide,
- iii) culturing the host organism obtained in step ii) under conditions suitable for expression of the polypeptide encoded by the polynucleotide or the vector; and optionally isolating from the host organism the polypeptide resulting from recombinant expression by the host organism.

42. (Amended) A method of diagnosing a clinical condition in an individual, said method comprising the steps of

- i) ~~performing the method of any of claims 30 to 41~~performing the method of claim 30, and
- ii) diagnosing the clinical condition.

53. (Amended) An inhibitory agent obtainable according to any to the method of ~~any of claims 49 to 52~~claim 49.

Claim 54 has been cancelled.

59. (Amended) An enhancing agent obtainable according to ~~any to the method of any of claims 54 to 57~~claim 54.

Claim 60 and 61 have been cancelled.

65. (Amended) The method according to ~~any of claims 63 and 64~~ claim 63, wherein the clinical condition is selected from the group consisting of Down's syndrome, preeclampsia and acute coronary syndrome, ~~including unstable angina and myocardial infarction.~~

66. (Amended) The method according to ~~any of claims 63 and 64~~ claim 63, wherein the complex is PAPP-A/promBP and the clinical condition is selected from the group consisting of Down's syndrome and acute coronary syndrome, ~~including unstable angina and myocardial infarction.~~

67. (Amended) The method according to ~~any of claims 63 and 64~~ claim 63, wherein the complex is promBP/ANG and the clinical condition is Down's syndrome.

Claims 68 and 69 have been added:

68. (New) A method of treating a clinical condition mediated by IGFBP-5 which comprises administering to a subject in need thereof a therapeutically effective amount of the polypeptide of claim 12.

69. (New) A method of treating a clinical condition mediated by PAPP-A2 which comprises administering to a subject in need thereof a therapeutically effective amount of the inhibitory agent of claim 53.